

**Claims**

What is claimed is:

1. A method for distinguishing between the presence of a target nucleic acid sequence and a variant of the target nucleic acid sequence in a test sample, wherein the variant nucleic acid contains a variation from the target nucleic acid sequence comprising a deletion of eight or more consecutive nucleotides, the method comprises the steps of:
  - a) contacting the test sample with amplification reagents and a first and second amplification primer to form a reaction mixture, wherein the first primer hybridizes with the target nucleic acid sequence at the site containing the variation in the variant sequence;
  - b) subjecting the reaction mixture to amplification conditions; and
  - c) detecting the presence of an amplification product from the first and second primers as an indication of the presence of the target nucleic acid sequence in the test sample.
2. The method of claim 1 wherein detecting the presence of the amplification product comprises hybridizing a labeled probe to the amplification product.
3. The method of claim 1 wherein a failure to detect an amplification product is an indication of the presence of the variant nucleic acid sequence in the test sample.
4. The method of claim 1 wherein
  - a) the reaction mixture further comprises a control nucleic acid sequence and primers for amplifying the control nucleic acid sequence, and
  - b) the method further comprises the step of detecting the amplified control nucleic acid sequence as an indication that the amplification reagents and conditions were efficacious for producing an amplification product.
5. The method of claim 4 wherein a failure to detect an amplification product is an indication of the presence of the variant nucleic acid sequence in the test sample.

6. The method of claim 4 wherein detecting the presence of the amplification product and detecting the amplified control nucleic acid sequence comprises hybridizing a first labeled probe to the amplification product and second labeled probe to the amplified control  
5 nucleic acid sequence.

7. The method of claim 4 wherein the control nucleic acid sequence is a sequence contained within a gene or pseudogene homologous to a gene containing the target nucleic acid sequence.

8. The method of claim 7 wherein one of the primers for amplifying the control nucleic acid sequence is selected from the first and the second primer.

9. The method of claim 1 wherein the test sample is from a patient and the method further comprises the step of altering the patient's medical care regimen based upon the presence or absence of the target sequence in the test sample.

10. The method of claim 1 further comprising the steps of:  
a) contacting the test sample with additional amplification primers and amplification reagents, wherein the amplification primers amplify a second target nucleic acid sequence and a variant of the second target nucleic acid sequence wherein the variant of the second target nucleic acid sequence contains a one to seven nucleotide variation from the second target nucleic acid sequence;  
b) subjecting the test sample and additional amplification primers and amplification reagents to amplification conditions to form a second amplification product; and  
c) detecting the presence of a second amplification product as an indication of the second target nucleic acid sequence or variant of the second target nucleic acid sequence in the test sample.

11. The method of claim 10 wherein the reaction mixture comprising amplification reagents and the first and second amplification primers, also includes the additional amplification primers and amplification reagents.

12. The method of claim 10 wherein detecting the presence of the amplification product and second amplification product comprises hybridizing a first labeled probe to the amplification product and a second labeled probe to the second amplification product.
13. The method of claim 10 wherein the first and second labeled probes are detected on the same apparatus.
14. The method of claim 10 wherein the variant of the second target nucleic acid sequence contains a single nucleotide variation.
15. The method of claim 10 wherein the target nucleic acid is a nucleic acid sequence within the cytochrome P-450 2D (*CYP2D*) family.
16. The method of claim 13 wherein the deletion is *CYP2D6*\*5 and the variant of the second target nucleic acid sequence is selected from *CYP2D6*\*3, *CYP2D6*\*4, *CYP2D6*\*6, and any combination of *CYP2D6*\*3, *CYP2D6*\*4, and *CYP2D6*\*6.
17. A method for detecting a target nucleic acid sequence in a test sample comprising the steps of:
- a) contacting the test sample with amplification reagents comprising a polymerase, a PCR primer pair, and a probe to form a reaction mixture;
  - b) performing the following cycle
    - (i) raising the temperature of the reaction mixture to a temperature sufficient to dissociate double stranded nucleic acid sequences,
    - (ii) lowering the temperature of the reaction mixture to allow the PCR primers and probe to hybridize to the nucleic acid and thereby form primer hybrids and probe hybrids,
    - (iii) raising the temperature of the reaction mixture to a temperature sufficient to dissociate the probe hybrids, if the probe is not completely complementary to the nucleic acid, but not sufficient to dissociate the primer hybrids,

(iv) raising the temperature of the reaction mixture to a temperature sufficient to activate the polymerase;

c) repeatedly performing the cycle of step b) to form an amplification product; and

d) detecting the amplification product as an indication of the presence of the nucleic acid sequence in the test sample.

18. The method of claim 17 wherein the target nucleic acid sequence is a polymorphic nucleic acid sequence.

19. A method for detecting the presence a deletion or an insertion in a target nucleic acid sequence in a test sample, wherein the deletion or insertion is at least 8 or more consecutive nucleotides, the method comprises the steps of:

a) contacting the test sample with amplification reagents and a set of amplification primers to form a reaction mixture wherein the set of amplification primers hybridize with the target nucleic acid sequence and a standard nucleic acid sequence in the test sample;

b) subjecting the reaction mixture to amplification conditions to form a target nucleic acid sequence amplification product and a standard nucleic acid amplification product;

c) hybridizing a first probe to the target sequence amplification product and a second probe to the standard nucleic acid sequence amplification product to form first probe/target sequence amplification product hybrids and second probe/standard nucleic acid amplification product hybrids;

d) detecting the hybrids; and

e) comparing the signals from the first and second labeled probes to determine the presence of the deletion or insertion in the target nucleic acid sequence in the test sample.

20. The method of claim 19 wherein the standard nucleic acid sequence is a nucleic acid sequence added to the reaction mixture.

21. The method of claim 19 wherein the standard nucleic acid sequence is a nucleic acid sequence within a gene or pseudogene homologous to a gene containing the target nucleic acid sequence.
22. The method of claim 19 wherein the first and second probes differ by a single nucleotide.
23. The method of claim 19 wherein the test sample is from a patient and the method further comprises the step of altering the patient's medical care regimen based upon the presence or absence of the target sequence in the test sample.
24. The method of claim 19 wherein the set of amplification primers comprises four amplification primers.
25. The method of claim 19 wherein the set of amplification primers comprises less than four primers and at least one primer of the set of amplification primers hybridizes to the target nucleic acid sequence and standard nucleic acid sequence.
26. The method of claim 19 further comprising the steps of:
- a) contacting the test sample with additional amplification primers and amplification reagents, wherein the amplification primers amplify a second target nucleic acid sequence and a variant of the second target nucleic acid sequence wherein the variant of the second target nucleic acid sequence contains a one to seven nucleotide variation from the second target nucleic acid sequence;
  - b) subjecting the test sample and additional amplification primers and amplification reagents to amplification conditions to form a second amplification product; and
  - c) detecting the presence of a second amplification product as an indication of the second target nucleic acid sequence or variant of the second target nucleic acid sequence in the test sample.

27. The method of claim 26 wherein the reaction mixture comprising the test sample, amplification reagents and a set of amplification primers, further comprises the additional amplification primers and amplification reagents.
28. The method of claim 26 wherein detecting the presence of the second amplification product amplification product comprises hybridizing a labeled probe to the second amplification product.
29. The method of claim 19 wherein the primers are labeled and detecting the hybrids comprises detecting the labeled primers that have been incorporated into the hybrids.
30. The method of claim 19 wherein the first and second probes are labeled and detecting the hybrids comprises detecting the labeled probes that have been incorporated into the hybrids.
31. The method of claim 28 wherein the first and second probes are labeled and detecting the hybrids comprises detecting the labeled probes that have been incorporated into the hybrids with the same apparatus employed to detect the second amplification product.
32. The method of claim 26 wherein at least one member of the primer set and the additional amplification primers are labeled and detecting the presence of the hybrids and second amplification product comprises contacting the amplification product, second amplification product, and standard nucleic acid sequence amplification product with probes immobilized to a solid support in an array.
33. The method of claim 26 wherein the first and second target nucleic acid sequences are nucleic acid sequences within *CYP2D* family.
34. The method of claim 33 wherein the deletion is \*5 and the variant of the second target nucleic acid sequence is selected from \*3, \*4, \*6, and any combination of \*3, \*4, and \*6.

35. The method of claim 26 wherein the test sample is from a patient and the method further comprises the step of altering the patient's medical care regimen based upon the presence or absence of the first or variant of the second target sequence in the test sample.
36. The method of claim 1 wherein the first or second amplification primer is labeled.
37. The method of claim 1 wherein the first or second amplification primer is labeled and a additional amplification primer is labeled.